

Danish 3R-Center



More than 140 participants. Please use the opportunity for networking. Presentations are covered and with abstracts and selected PDFs of presentations.

Annual meeting as a 2 day symposium –

This year with several European speakers



Program 10th November

News from 3R centres and activities

DK: European engagement, survey, teaching, 3R prize, grants

NC3R: More than 10 years 20 employed, supported 238 major awards, active interaction with researchers, SMEs, industry Acute tox study with impact on ICH M3 guideline, Data sharing, Arrive, Crack it, ExpDesignerAssistant. Discussion about inclusion of animal welfare organisations



Program 10th November

News from 3R centres and activities

Århus: Symposium on Metaanalysis 16+17.
November

Novo Nordic: 4 persons engaged in new 3R
unit focusing on internal projects and
internal collaborations. First in the world.
Established on ethical grounds.



Program 10th November

News from 3R centres and activities

Presentation of last years 3R projects supported by the 3R centre:

Polyclonal antibodies in chicken – Otto Kalliokoski

In vitro human skin model – Mette Elena Skindersø

In vitro model to predict lung toxicity – Søren Thor Larsen



'Home' Teaching material for high school from 3R centre

Danmarks 3R-Center

RRR

Om 3R-centeret Forskning 3R Internationalt 3R Arrangementer Forsøgsdyr English Søg

Undervisningsmateriale om forsøgsdyr og de 3R'er

Undervisningsmaterialet er tiltænkt de gymnasiale uddannelser i fagene Biologi A og Bioteknologi A.

Undervisningsforløb

Vigtigt: Læs lærervejledningen og følg derefter undervisningsmaterialets 5 trin:

1. Quiz - første del (send dit navn til ranon@fvst.dk og modtag login til quiz indenfor to arbejdsdage)
2. [Forsøgsdyr og 3R](#) (film)
3. [3R - vejen mod færre og mere skånsomme dyreforsøg](#) (baggrundsartikel)
4. Gruppearbejde med udgangspunkt i [ressource-rummet](#).
5. Quiz - anden del

(Undervisningsmaterialet bliver i nærmeste fremtid suppleret med yderlige to artikler)

Vejledning

- [Lærervejledning](#)
- [Quizvejledning](#)

Ophavsret og kreditering

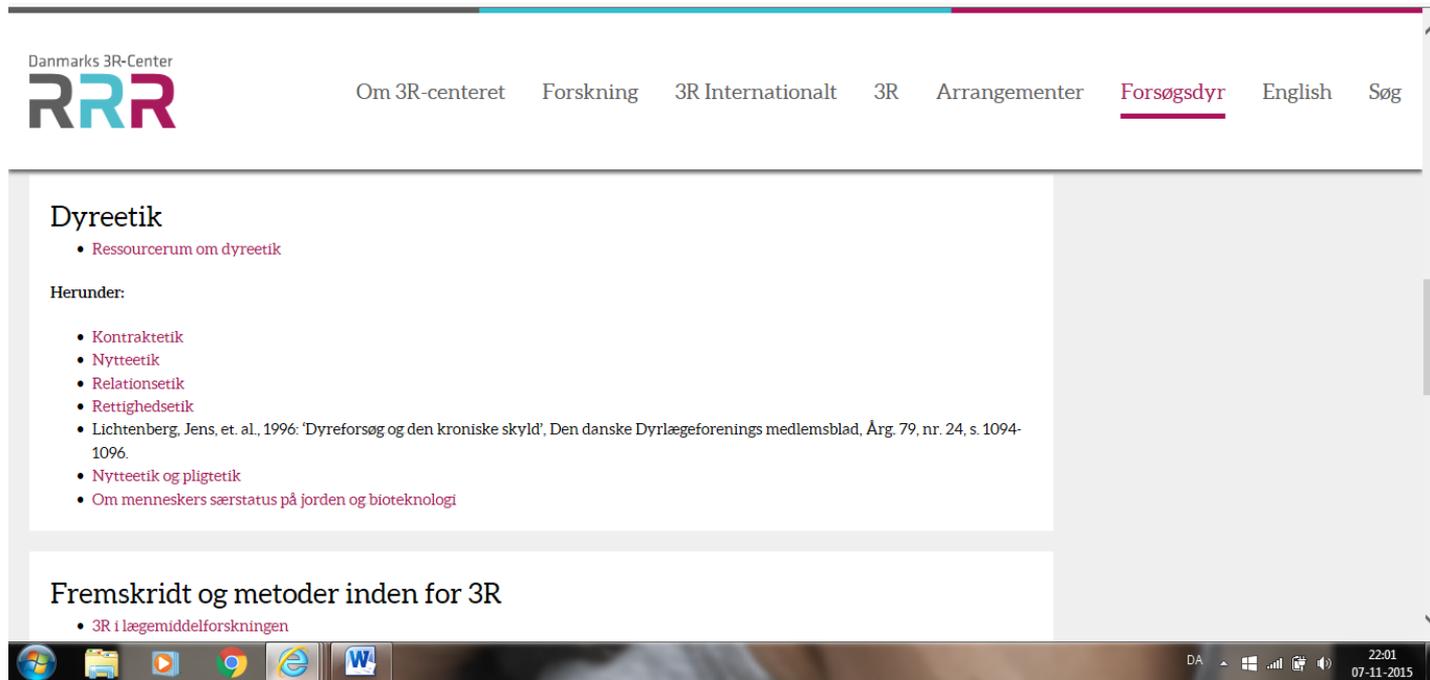
Ophavsretten til materialet ligger hos Danmarks 3R-Center

Freelancejournalist Aiko Sho Nielsens navn skal fremgå af materialet i forbindelse med enhver offentliggørelse

Windows taskbar: 22:00 07-11-2015



'Resource room' – group assignments (detailed and deeper understanding)



The screenshot shows the website of the Danmarks 3R-Center. The header includes the logo 'RRR' and a navigation menu with items: 'Om 3R-centeret', 'Forskning', '3R Internationalt', '3R', 'Arrangementer', 'Forsøgsdyr' (underlined), 'English', and 'Søg'. The main content area is titled 'Dyreetik' and contains a list of resources under the heading 'Herunder:'. The list includes links to 'Kontraktetik', 'Nytteetik', 'Relationsetik', 'Rettighedsetik', a citation by Lichtenberg et al. (1996), 'Nytteetik og pligtetik', and 'Om menneskers særstatus på jorden og bioteknologi'. Below this, there is a section titled 'Fremskridt og metoder inden for 3R' with a link to '3R i lægemiddelforskningen'. The Windows taskbar at the bottom shows the time as 22:01 on 07-11-2015.

Danmarks 3R-Center
RRR

Om 3R-centeret Forskning 3R Internationalt 3R Arrangementer Forsøgsdyr English Søg

Dyreetik

- Ressourcerum om dyreetik

Herunder:

- Kontraktetik
- Nytteetik
- Relationsetik
- Rettighedsetik
- Lichtenberg, Jens, et. al., 1996: 'Dyreforsøg og den kroniske skyld', Den danske Dyrlægeforenings medlemsblad, Årg. 79, nr. 24, s. 1094-1096.
- Nytteetik og pligtetik
- Om menneskers særstatus på jorden og bioteknologi

Fremskridt og metoder inden for 3R

- 3R i lægemiddelforskningen

22:01
07-11-2015



The 3Rs: on animal scientists' perceptions, awareness and practices

Overall aim: to improve the basis for further implementation of the 3Rs in Denmark and establish a baseline for assessing future implementation

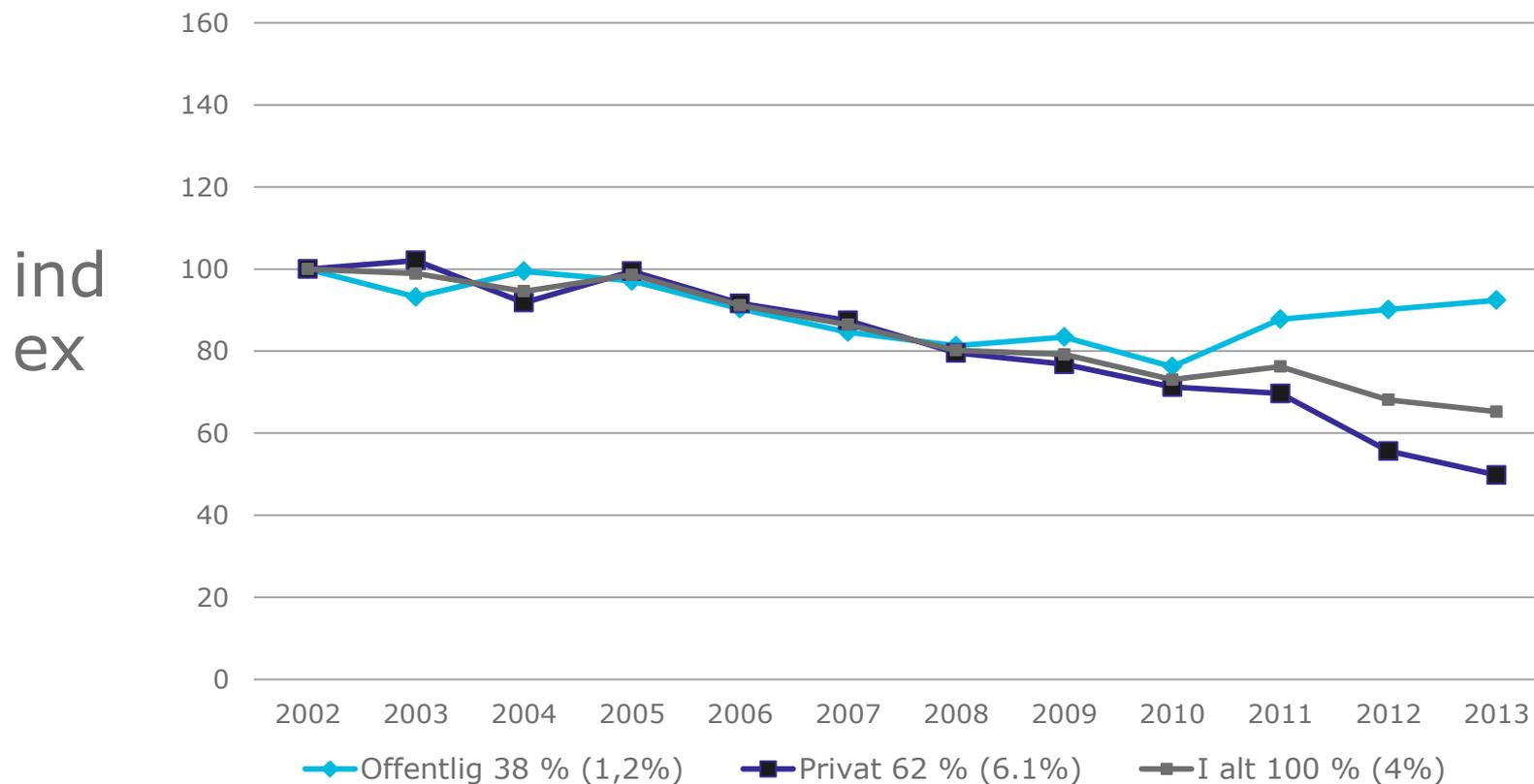
Research questions

1. What is the level of awareness and knowledge about the 3Rs among Danish animal scientists?
2. To what extent are the 3Rs implemented in practice?
3. What are the barriers for further implementation?



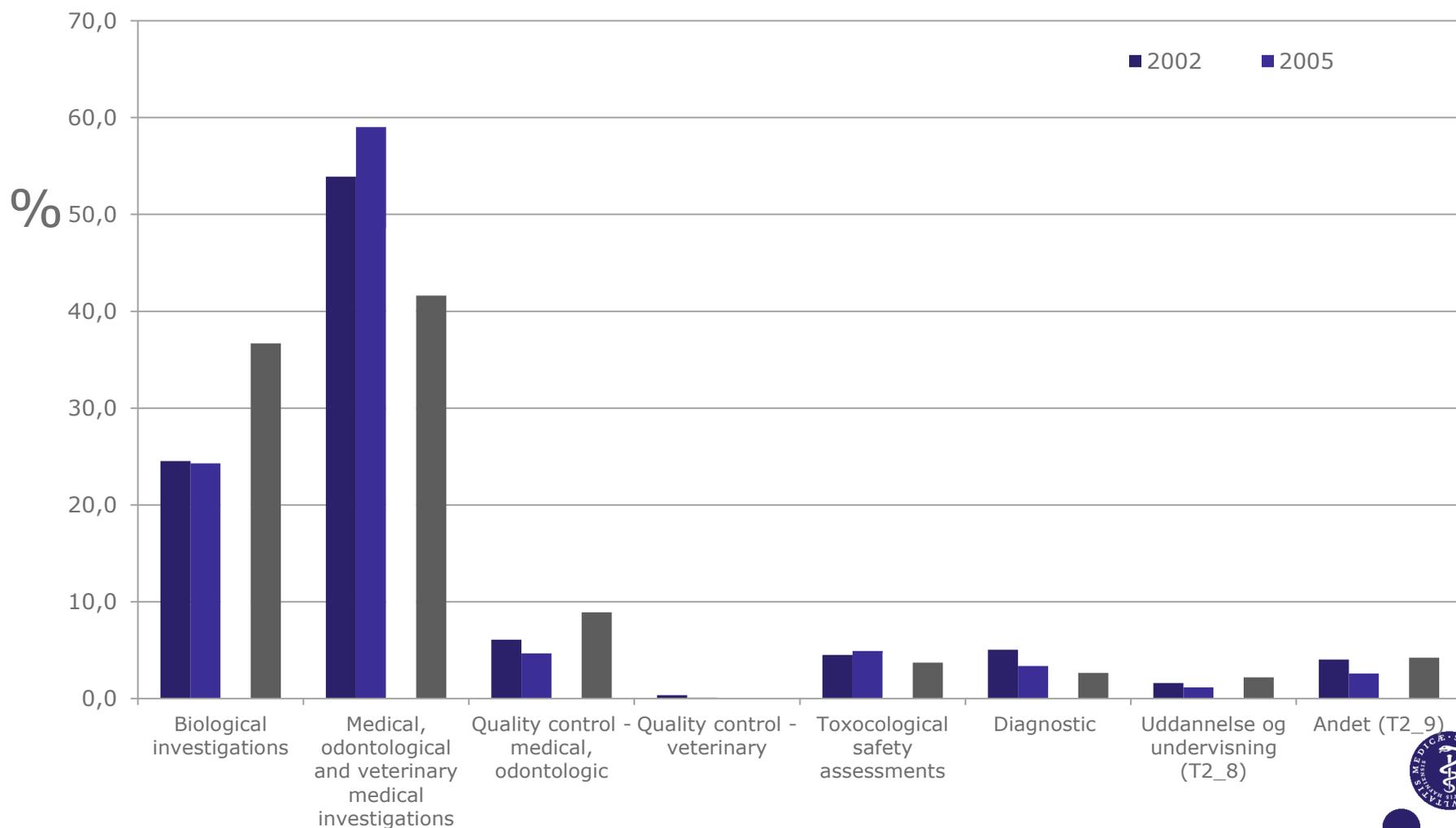
Preliminary findings

Number of animals used



Preliminary findings

Types of investigations – selected years



Animal use for science in Europe. [Daneshian M, Busquet F, Hartung T, Leist M. ALTEX. 2015;32\(4\):261-74.](#)

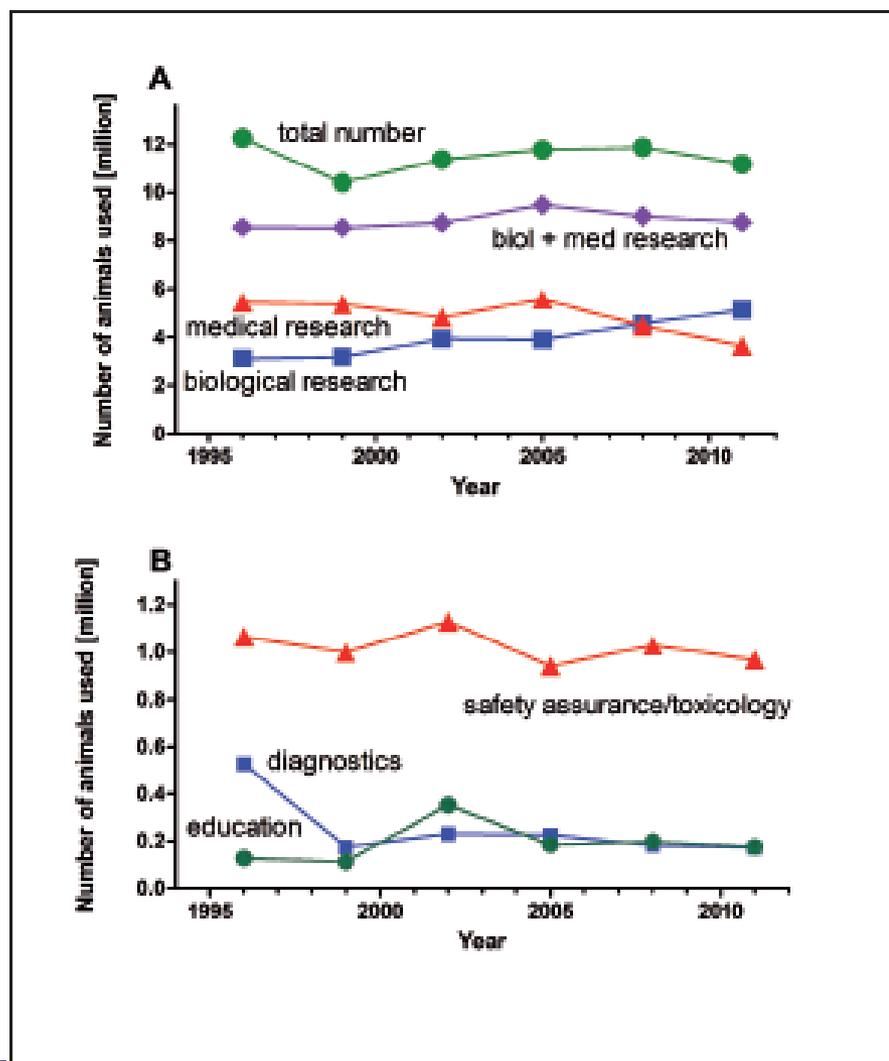


Fig. 1: Numbers of animals used for scientific purposes in 16 core European countries

Data obtained from European Commission reports on the statistics on the number of animals used for experimental and other scientific purposes in Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxemburg, Portugal, Spain, Sweden, Switzerland, The Netherlands and United Kingdom for the years 1996, 1999, 2002, 2005, 2008 and 2011; corresponding data from Switzerland were obtained from the Swiss federal food safety and veterinary office; (A) Total number of animals used (green circles), and detail numbers for research and development for medicine, veterinary and dentistry, summarized as medical research (red triangles), biological research, which refers to basic biological research (blue squares) and medical + biological research combined (purple diamonds). (B) The proportion of animals used for the purpose of safety assurance, i.e., toxicological testing (red triangles), for diagnostic (blue squares) and education purposes (green circles).



Animal use for science in Europe. [Daneshian M](#), [Busquet F](#), [Hartung T](#), [Leist M](#). *ALTEX*. 2015;32(4):261-74.

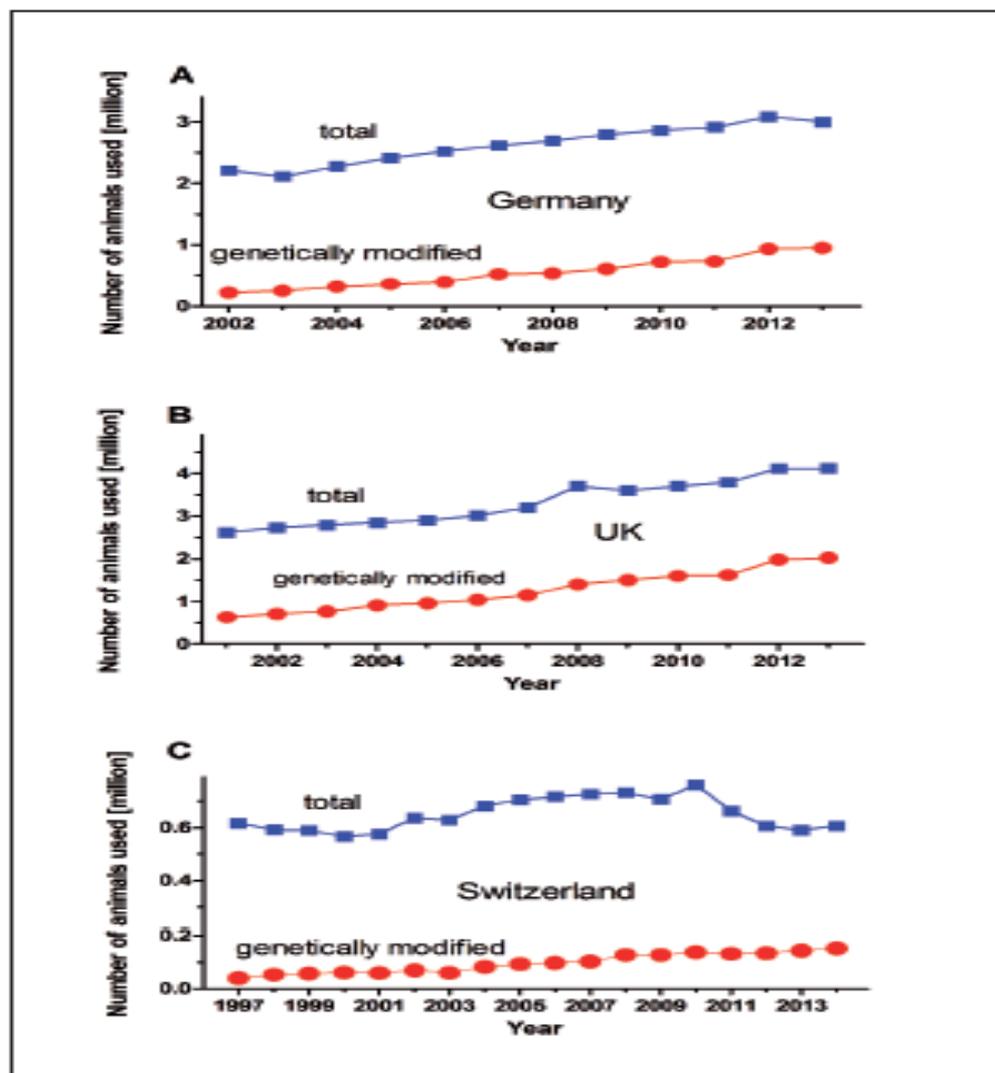


Fig. 2: National examples for the number of transgenic and non-transgenic animals used for scientific purposes. The total annual number of animals (blue squares) and genetically-modified animals (red circles) in (A) Germany, (B) UK and (C) Switzerland. Data are from annual publications on statistics on animals used for scientific purposes from the German Federal Ministry of Food and Agriculture (BMEL), the UK Home Office and the Swiss Federal Food Safety and Veterinary Office (BLV).

Animal use for science in Europe. [Daneshian M, Busquet F, Hartung T, Leist M. ALTEX. 2015;32\(4\):261-74.](#)

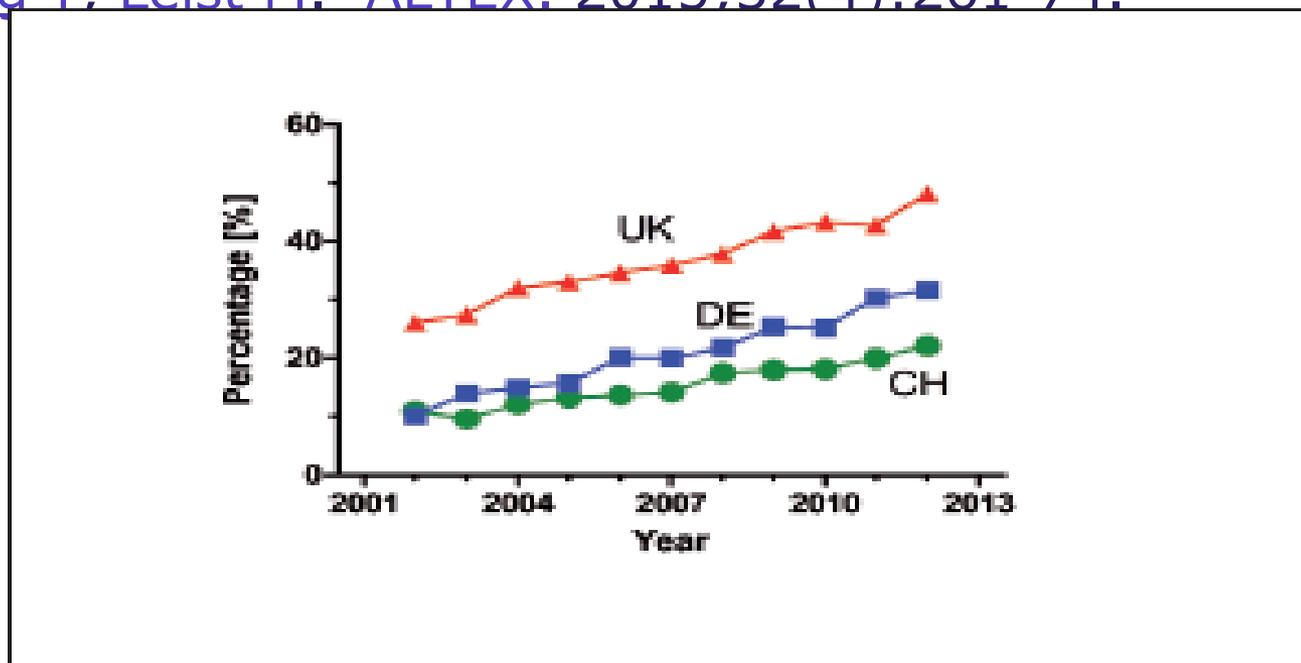


Fig. 3: Proportion of genetically modified animals of the total number of animals

The graph shows the annual percentage of transgenic animals of the total animals used for scientific purposes from 2002 to 2012 in the United Kingdom (UK, red triangles), Germany (DE, blue squares) and Switzerland (CH, green circles). Data are calculated from annual publications on statistics on animals used for scientific purposes from the German Federal Ministry of Food and Agriculture (BMEL), the UK Home Office and the Swiss Federal Food Safety and Veterinary Office (BLV).

Posters presented

Al-Malahmeh et al, Wagening University: Physiologically based kinetic modelling of bioactivation of myristirum facilitating risk assessment

Yishi Huang et al, Dansih Nanosafe Centre: The constrained drop surfactometer as a toll for toxicological assessment of impregnation spray products

Alayjlouni AM et al, Wagening: Mode of action based risk assessment of the botanical food-borne alkenylbenzene apiol from parsley using physiologically based kinetic (PBK) modelling and read across to safrole



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Animals used for scientific purposes

Legislation and implementation

The "Three Rs" and alternative approaches

Replacement, Reduction and Refinement – the "Three Rs"

Validation, acceptance and use

EU activities to advance alternatives

Member State activities to advance alternatives

Finding and distributing information on alternatives

Key resources

[Search Tools](#)[Databases](#)[Portals and web-sites](#)[Journals](#)[Other resources and organisations](#)

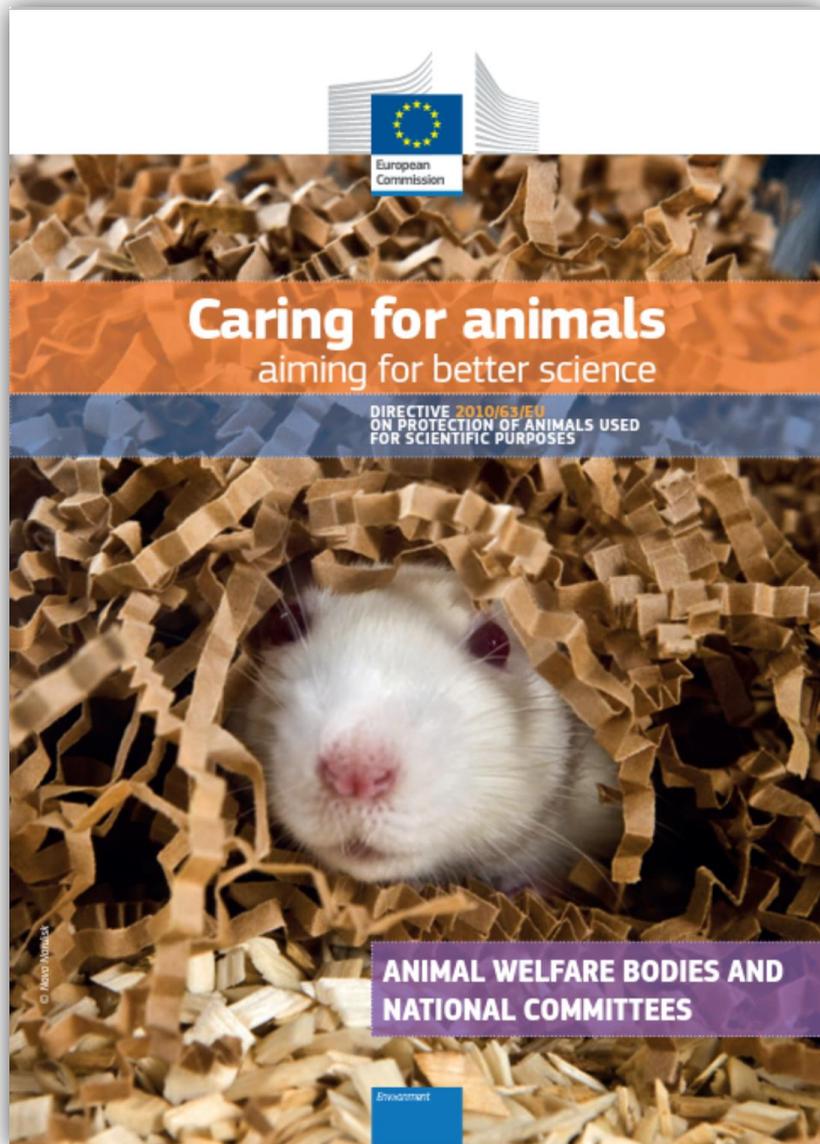
Animals used for scientific purposes



Search Tools

- [EURL ECVAM Search Guide \(the Guide\)](#) – The Guide is particularly helpful to inexperienced database users. It represents a useful resource where comprehensive searches for alternatives are required as part of authorisation processes for animal experiments and where regulatory requirements mandate the application of the Three Rs. The Guide provides examples of search procedures and user guidance to facilitate the location of the desired information on Three Rs alternatives; it also includes an inventory of relevant resources, contains a check list (the seven golden steps) to allow for searches in a structured and systematic manner, moreover, search principles, suggested search terms etc. Free copies of the handbook or a pdf version are available from the [EU Bookshop](#).
- [Go3R](#) - is a free of charge 'semantic' search engine making use of underlying expert knowledge on 3Rs methods to specifically retrieve Three Rs-relevant information. Currently, the semantic Go3R tool searches in the databases PubMed and TOXNET. Additionally, Go3R allows searching the entire World Wide Web using a Google search with automatic higher ranking of 3Rs relevant websites. Results of PubMed and TOXNET searches are presented to the user together with a dynamic table of contents highlighting 3Rs information and allowing to quickly restrict vast search results to relevant documents. The Go3R expert knowledge covers the entire scientific domain of alternatives to animal testing in all biomedical disciplines, but has a special focus on regulatory toxicity testing.
- [Search.norecopa.no](#) is a search engine for Norecopa's four [databases](#): [3R Guide](#), [NORINA](#), [TextBase](#) and [Classic AVs](#). The search engine takes into consideration the words which have been entered by the user; an index of all the words in the databases; a list of synonyms constructed specifically for these databases; an "auto-complete" function which suggests search terms based on the search engine's own dictionary; algorithms which prioritise or suppress words depending on their relevance; Boolean operators, which the user can edit and "fuzzy logic" (words resembling those entered by the user). The user can limit the search to one or more of Norecopa's four databases, or to one or more of a variety of search fields and scientific disciplines.

Last updated: 26/10/2015 | [Top](#)



However..

“Simply meeting the legislative requirements will **not** ensure appropriate welfare, care and use practices”

Requires **commitment**

Commitment enabled through **institutional support**

Institutional support facilitated via **regulatory support**



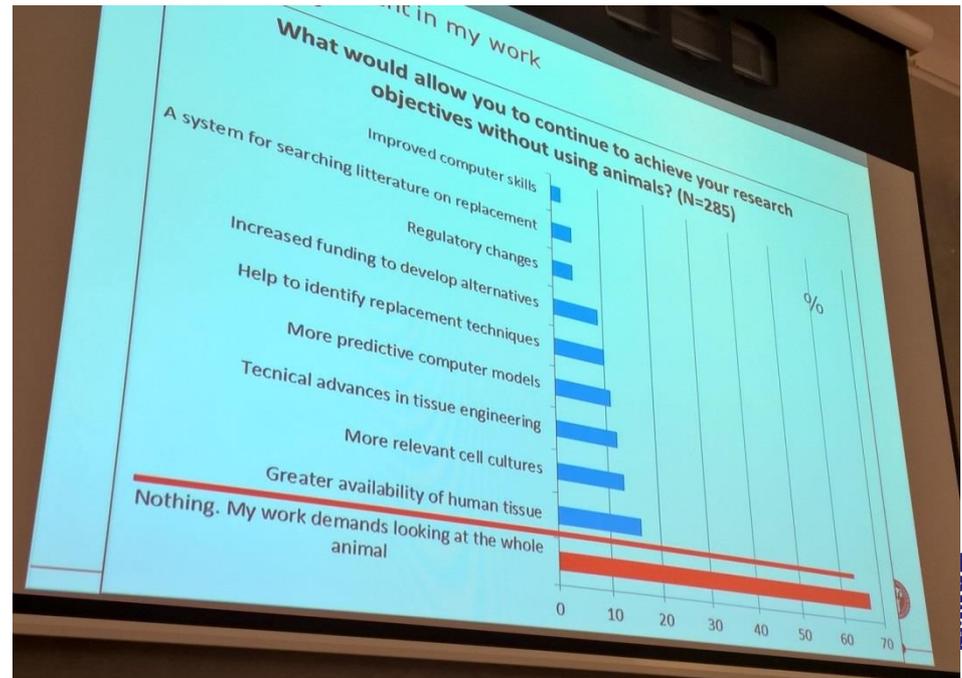
Culture of Challenge

Challenge – the path for discovery

Researcher

- **Right questions?**
- **Right disciplines?**
- **Right models?**
- **Beyond obvious?**

- **Refinement..**



Conclusions

Legal framework, partners and networks in place to strive strategically for new alternative approaches – **take part**

From aspiration to practical, continued implementation of the Three Rs

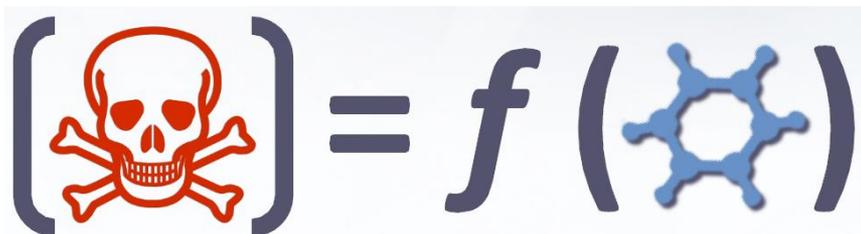
Three Rs is **everyone's responsibility**

Time to roll out **Culture of Challenge**
- for the benefit of science and animals

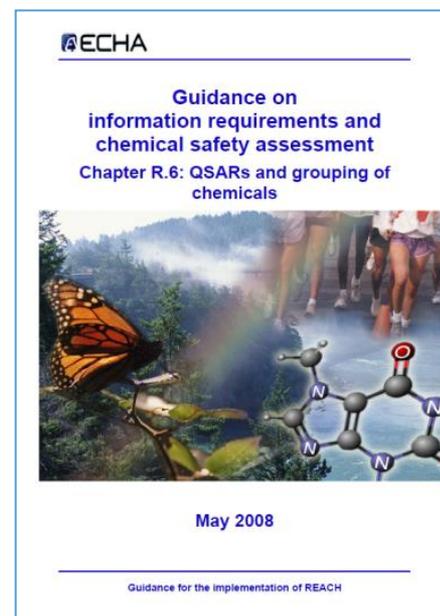


Definition of QSAR: Quantitative Structure-Activity Relationship

A QSAR is a mathematical model (often a statistical correlation) relating one or more parameters derived from chemical structure to a property or activity, e.g. a toxicological endpoint



See e.g. **EU chemicals legislation, REACH, guidance R.6:**
"QSARs and grouping of chemicals" for more information
http://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf



New Danish QSAR predictions database

Danish (Q)SAR Database

powered by [OASIS Database](#)

[Setup information](#)

[Tutorial and demonstration movies](#)

[Getting started](#)

[Information on the models used \(PDF\)](#)

Searching requires that you have Java 5 or higher installed.

You can get the most current version of the Java Runtime at <http://java.sun.com/getjava/>.

Start search

[Search sections and basic clauses](#)

[Combined clauses](#)

[Defining a clause](#)

[Adding a clause](#)

[Executing a clause](#)

[Search Results](#)

[Saving / loading query trees](#)

[Search examples](#)

[CAS search](#)

[Name search](#)

[Database affiliation search](#)

[Parameter search](#)

[More search examples](#)

[Alkyl example](#)

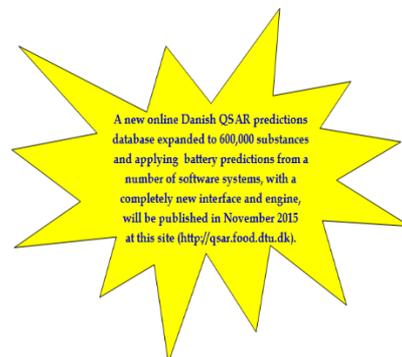
[Quaternary nitrogen example](#)

[Aldehydes example](#)

[Wildcard atom example](#)

[Specific wildcard atom \(atom list\) example](#)

Your comments and questions are welcome. For more information, please contact [LMC](#)



New search
Searches
Results
Substances

Id

PhysChem

Environment

ADME

Human health

Structure

AND
Intersect results

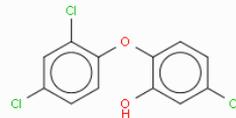
OR
Unite results

NOT
Complement results

RN: 3380-34-5: Page 1

Previous Next

Extra columns



3380-34-5

Download

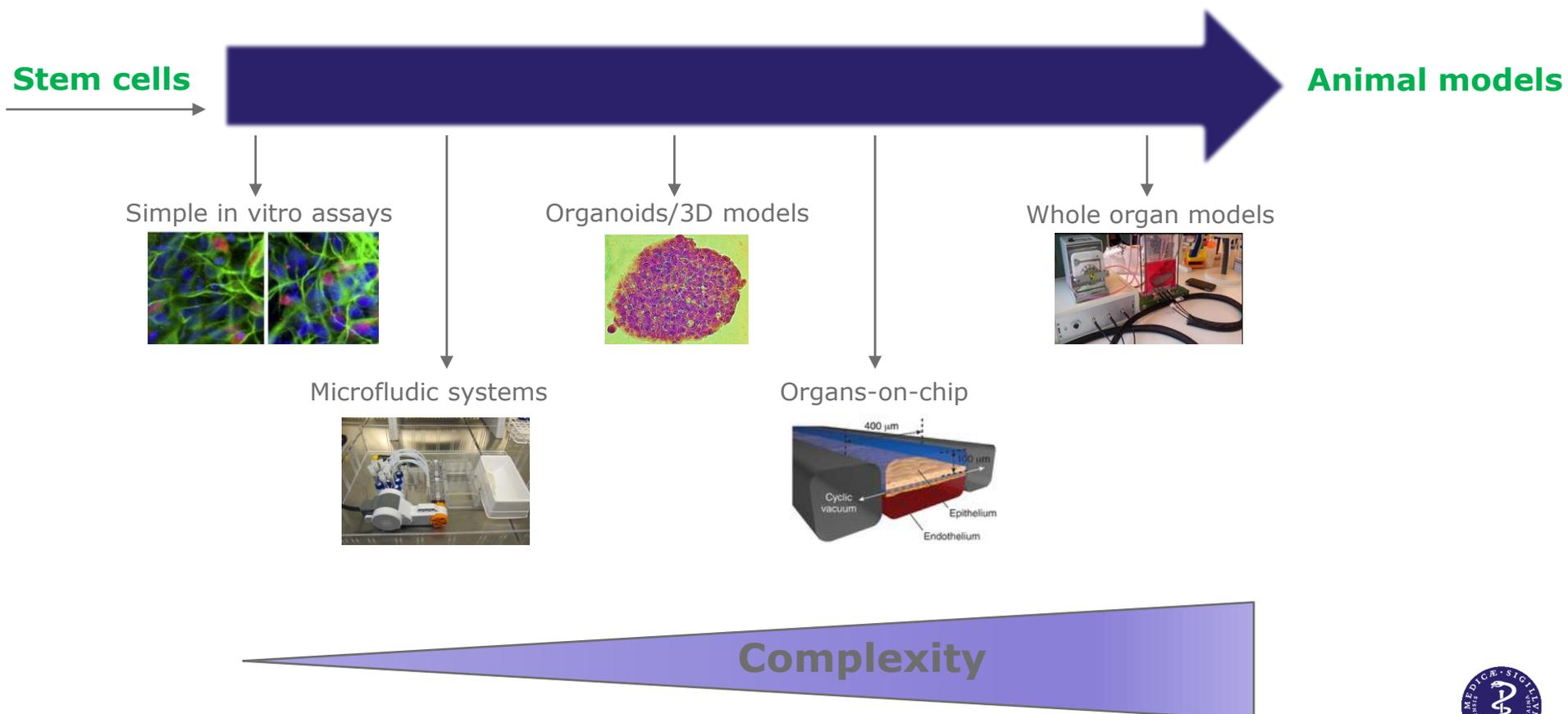
Irritation and Sensitisation				
	Battery	CASE Ultra	Leadscope	SciQSAR
Severe Skin Irritation in Rabbit	NEG_IN	INC_OUT	NEG_IN	NEG_IN
Allergic Contact Dermatitis in Guinea Pig and Human	POS_IN	POS_IN	NEG_IN	POS_IN
Respiratory Sensitisation in Humans	POS_OUT	INC_OUT	POS_OUT	POS_IN

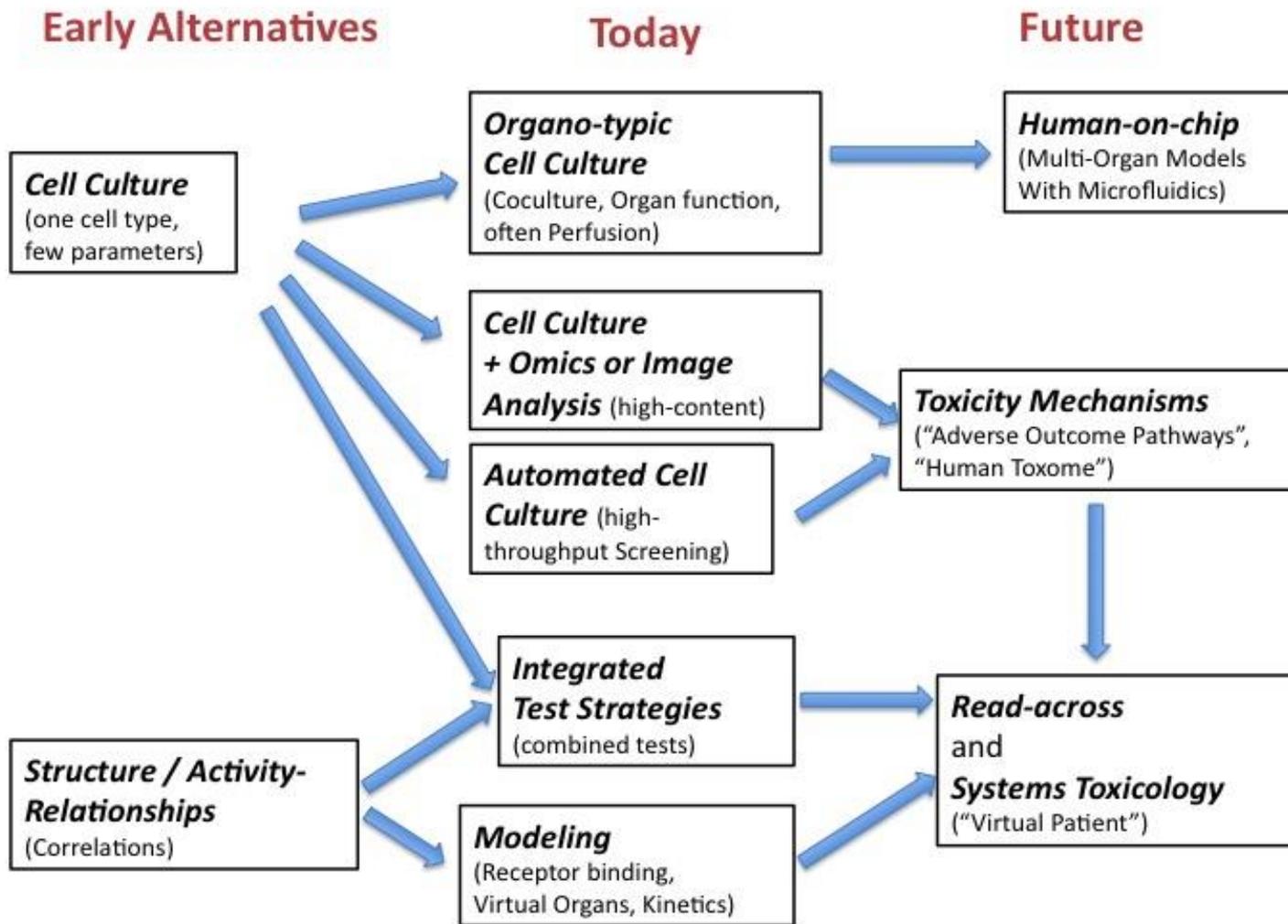
Endocrine and Molecular Endpoints				
	Battery	CASE Ultra	Leadscope	SdQSAR
Estrogen Receptor α Binding ALL (Human in vitro)	NEG_IN	NEG_IN	NEG_IN	POS_IN
Estrogen Receptor α Binding BAL (Human in vitro)	INC_OUT	NEG_IN	NEG_OUT	POS_IN
Estrogen Receptor α Activation (Human in vitro)	NEG_IN	NEG_IN	NEG_IN	POS_IN
Androgen Receptor Antagonism (Human in vitro)	POS_IN	POS_IN	POS_IN	POS_IN
Thyroid Receptor α Binding -log(IC50 in μ M) (Human in vitro)	-2.521545	-5.204	-2.69239	-2.3507
Thyroid Receptor β Binding -log(IC50 in μ M) (Human in vitro)	-2.44499	-4.51	-1.22557	-1.5994
Pregnane X Receptor (PXR) Binding (human in vitro)	INC_OUT	NEG_IN	NEG_OUT	POS_IN





Stem cells as tools to address the 3Rs





CAAT 2.1 – a vision and a strategy led by Thomas Hartung



Hannes remarks

Awareness internally and externally of lab animals welfare through education, communication and dialogic

Review of a lot of applications for permits and of protocols of animal experimentation

Stop for the use of many thousands of mice, rats, rabbits for batch control of efficacy and purity of insulins glucagons, growth hrne and FVII

Stop for use of thousands of mice for production of monoclonal antibodies by the ascites method

Inroduction and use of better anesthesia and analgesia

Improvement of housing and environmental enrichment

My 1 priority as lab animal vet has been to be available for the animals, the animal technicians and the scientists



Announcement of Workshops 14-18 August 2016 at Panum, University of Copenhagen with 3R

Bridging genomics, human environmental health risk assessment and the 3Rs in animal science

to be organized by the Nordic Environmental Mutagen Societies (NordEMS) and adhered to program of the European Environmental Mutagen Societies (EEMS), and European Concensus Platform of Alternatives (ECOPA) in August 2016 in Copenhagen.

Organising committee: Lisbeth E. Knudsen, University of Copenhagen, Denmark (chair)

Jørn A. Holme, Norwegian Institute of Public Health, Head of Norwegian Society of Pharmacology and Toxicology (NSFT)

Margareta Törnqvist, Stockholm University, Sweden

Tuula Heinonen, president of FICAM and SSCT, Finland

Kristín Ólafsdóttir, University of Iceland

